REMARKS

I. Preliminary Remarks

Applicants wish to thank the Examiner for the courtesy shown to the undersigned attorney and to Dr. Christophe Reymond during the personal interview conducted August 26, 2009. During that interview amendments to independent claim 55 were discussed to clarify that the method of the invention generates and screens multiple sets of contiguous overlapping peptides (COPs) as distinguished from the prior art which might produce COPs but which do not carry out the generation and screening of multiple sets of such COPs according to the methods of the invention. Claim 55 is also amended to recite that the COPs comprise the entire amino acid sequence of the allergen.

The present invention relates generally to immunotherapy methods providing reduced risk of anaphylaxis. In particular, the invention is directed to the preparation of improved compositions of contiguous overlapping peptide fragments (COPs) for selected allergens wherein the fragments are capable of inducing a T cell response in patients who are hypersensitive to the allergen but wherein administration of the compositions of the invention results in reduced levels of IgE stimulation activity.

According to this method, COPs are generated by the steps of: (1) determining candidate sets of contiguous overlapping peptides by a method comprising: (a) conducting a structural analysis of the selected allergen; (b) selecting one or more separation sites to provide sets of contiguous overlapping peptide fragments greater than 30 peptides in length which are linear and which peptides overlap each separation site; (2) producing said sets of candidate contiguous overlapping peptide fragments; and (3) screening said sets of candidate COPs by the steps of: (a) selecting sets of COPs characterized by having a T cell stimulating activity for T cells specific for the selected polypeptide allergen which is greater than a selected minimum; and (b) selecting sets of COPs characterized by having an IgE binding activity for IgE's reactive with the selected polypeptide allergen which is less than a selected maximum.

Reamendment of SEQ ID NO: 5 was also discussed at the invitation of the Examiner to re-correct an obvious typographical error. Specifically, amino acids 1 to 90 (namely up to seq ...SVIEGG) is the proper sequence of the Bet v 1 fragment as may be seen by

comparison with SEQ ID: 7. Applicants have discovered that part of Part of SEQ ID: 4 (PLA2 sequence) was inadvertently added thereafter, namely starting with HPVT... and ending with ...DLRKY to produce an erroneous sequence.

This error is obvious, and its solution is the deletion of amino acids 91 to 125 of the former SEQ ID NO: 5 (see Exhibit A attached hereto). As pointed out by the Examiner this is obvious from the designation at para [0108] that SEQ ID NO: 5 is a Bet v 1 fragment that comprises 90 amino acids and a study of SEQ ID NO: 7 which presents the entire Bet v 1 amino acid sequence with a different but correct set of amino acids for 91 to 125. It is also obvious from a study of SEQ ID NO: 6 which overlaps with both SEQ ID NO: 5 and SEQ ID NO: 7 at amino acid number 81 through amino acid number 90 of those sequences that SEQ ID NO: 5 should include that same sequence of amino acids through amino acid 90 but that amino acid residues 91-125 are incorrect. Finally, a review of SEQ ID NO: 4 which is to a completely different antigen (PLA_2 not Bet v 1) demonstrates the erroneous nature of SEQ ID NO: 5 as filed.

A substitute sequence listing which identifies the correct sequence for SEQ ID NO: 5 is submitted herewith. As discussed above, the amendment to the SEQ ID NO: 5 corrects an obvious error and does not add new matter. A sequence statement pursuant to 37 C.F.R. § 1.825(a) and (b) is also submitted herewith.

II. Outstanding Rejections

Claims 55-61 and 63 have been rejected under 35 U.S.C. §102(b) as being anticipated by Spertini WO 01/88085.

Claims 55 and 61-62 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Spertini WO 01/88085 in view of Shanti et al., The Journal of Immunology, Vol. 151, 5354-5363, No. 10, 11/15/1993.

Claims 55, 63 and 65 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Spertini WO 01/88085 in view of Spertini et al., C23 Abstract AAAI presented at AAAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in J. Allergy Clin. Immunol., 105(1- pt. 2):S278.

III. Patentability Arguments

A. The Rejections of Claims 55-61 and 63 Under 35 USC §102 as being Anticipated Over Spertini WO 01/88085 Should Be Withdrawn.

WO 01/88085 discloses some of the individual elements of independent claim 55 but fails to disclose their combination in the order and manner of the invention to yield an improved method for generating sets of contiguous overlapping peptides (COPs).

While COPs useful for immunotherapy share certain characteristics the art including WO 01/88085 does not disclose applicant's method for selecting useful COPs. COPs have been identified empirically in the past and are characterized by possessing the properties of having 1) T cell stimulating activity for T cells specific for the selected allergen but 2) having weak binding activity for IgE's reactive with the selected allergen.

What the Applicant has contributed is a systematic method by which sets of useful COPs can be identified and generated for a polypeptide allergen. Thus, the first steps of Applicant's invention are (1)(a) conducting a structural analysis to identify three dimensional structural formations of the allergen followed by (1)(b) selecting one or more separation sites within the sequence of the polypeptide allergen to provide COPS presenting T-cell structural motifs but not tertiary structural motifs such that the overlapping peptide fragments do not bind or weakly bind IgE.

The Action cites to portions of WO 01/88085 relating to polypeptide fragments of various lengths (page 2) and that proteins or variant peptides "can tolerize or anergize appropriate T-cell subpopulations" (page 19, lines 14-15). However, the reference does not teach the element of "selecting separation sites" to produce sets of COP's presenting "potential T-cell epitopes but not alpha helix and beta-sheet structural motifs..." as claimed. In fact, WO 01/88085 states only that the administration of its Api m 6 proteins, peptides or variants "may result in lower levels of IgE stimulation." (page 19, lines 25-26, emphasis supplied) This indicates a hit or miss quality to the prior art method which does not disclose the claimed element of affirmatively selecting separation sites whereby lower levels of IgE would be obtained.

WO 01/88085 also fails to disclose screening sets of candidate COPs according to the invention. Specifically, WO 01/88085 discloses testing a peptide for T-cell stimulating activity but does not disclose testing multiple sets of COPs (that is multiple peptides) for such activity. Similarly, WO 01/88085 discloses testing of peptides for IgE-mediated immune responses but fails to disclose testing multiple sets of COPs or the screening and selecting of multiple sets of COPs having a greater than minimum T cell stimulating activity and a less than a selected maximum of IgE binding activity.

B. The Rejections of Claims 55, and 61-62 Under 35 USC §103(a) in view of Spertini WO 01/88085 in view of Shanti et al. Should Be Withdrawn.

The rejection of claims 55 and 61-62 under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 in view of Shanti et al. (The Journal of Immunology, Vol. 151, 5354-5363, No. 10, 11/15/1993) should be withdrawn because Shanti discloses dot blotting but fails to make up for the deficiencies of WO 01/88085 with respect to independent claim 55 as described above.

C. The Rejections of Claims 55, 63 and 65 Under 35 USC §103(a) in view of Spertini et al. WO 01/88085 in View of Spertini C23 Should Be Withdrawn.

The rejection of claims 55, 63 and 65 under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 in view of Spertini et al. C23 Abstract AAAI presented at AAAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in J. Allergy Clin. Immunol., 105(1- pt. 2):S278 should be withdrawn because Spertini C23 which discloses intradermal skin testes neither makes up for the deficiencies of WO 01/88085 with respect to the elements of independent claim 55 from which dependent claims 63 and 65 depend.

CONCLUSION

For the foregoing reasons, it is submitted that each of claims 55-63 and 65 should now be allowed. Should the Examiner wish to discuss any issues of form or substance, she is invited to contact the undersigned attorney at the number below.

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Respectfully submitted,

By 

Jeffrey S. Sharp
Registration No.: 31,879
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant

Exhibit A

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                                1         10         20         30         40         50
                                |         |          |          |          |          |
SEQ ID  4          IIYPGTLWCGHGNKSSGPNELGRFKHTDACCRTHDMCPDVMSAGESKHGLTNTASHTRL
OLD SEQ 5          ---------MGVFNYETEATSVIFAARLFKAFILDGDNLFPKVAPQAISSVENIEGNGG
NEW SEQ 5          ---------MGVFNYETEATSVIFAARLFKAFILDGDNLFPKVAPQAISSVENIEGNGG
SEQ ID  6          ------------------------------------------------------------
SEQ ID  7          ---------MGVFNYETEATSVIFAARLFKAFILDGDNLFPKVAPQAISSVENIEGNGG

                                60         70         80         90         100        110
                                |          |          |          |          |          |
SEQ ID  4          SCDCDDKFYDCLKNSADTISSYPVGKMYFNLIDTKCYKLEHPVTGCGERTEGRCLHYTVD
OLD SEQ 5          PGTIKKISFPEGFPFKYVKDRVDEVDHTNFKYNYSVIEGGHPVTGCGERTEGRCLHYTVD
NEW SEQ 5          PGTIKKISFPEGFPFKYVKDRVDEVDHTNFKYNYSVIEGG----------------------
SEQ ID  6          ------------------------------KYNYSVIEGGPIGDTLEKISNEIKIVATPD
SEQ ID  7          PGTIKKISFPEGFPFKYVKDRVDEVDHTNFKYNYSVIEGGPIGDTLEKISNEIKIVATPD

                                120        130        140        150        160        170
                                |          |          |          |          |          |
SEQ ID  4          KSKPKVYQWFDLRKY------------------------------------------------
OLD SEQ 5          KSKPKVYQWFDLRKY------------------------------------------------
NEW SEQ 5          ------------------------------------------------------------
SEQ ID  6          GGSILKISNKYHTKGDHEVKAEQVKASKEMGETLLRAVESYLLAHSDAYN----------
SEQ ID  7          GGSILKISNKYHTKGDHEVKAEQVKASKEMGETLLRAVESYLLAHSDAYN----------
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